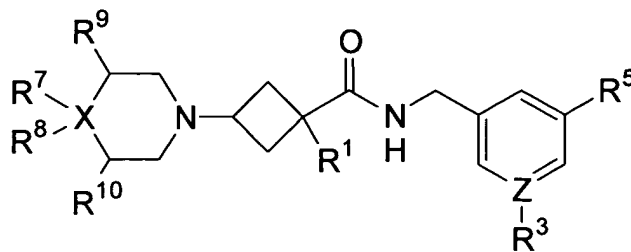


Amendments to the Claims:

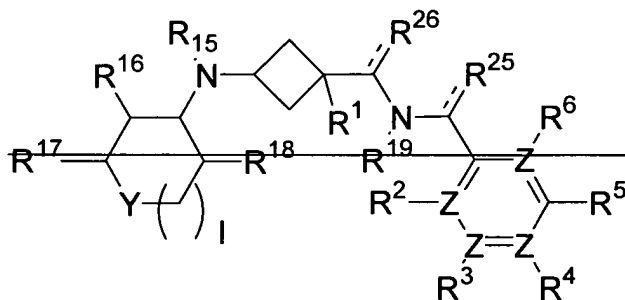
This listing of claims will replace all prior versions, and listings, of claims in this application.

Listing of Claims:

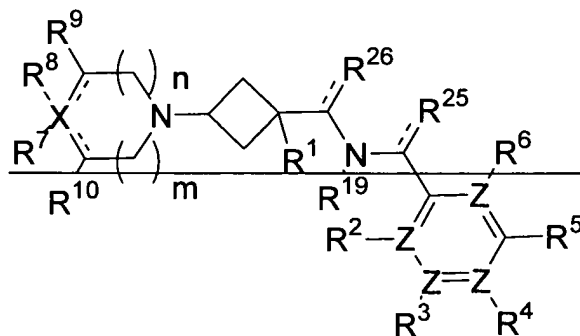
1. (Currently Amended) A compound of formula I ~~or formula II~~ IIa:



IIa



I



II

wherein:

X is O, N, S, SO₂ or C;

Y is selected from: O, NR¹², S, SO, SO₂, and CR¹²R¹², NSO₂R¹⁴,
~~NCOR¹³, CR¹²COR¹¹, CR¹²OCOR¹³ and CO;~~

R¹¹ is selected from: hydroxy, hydrogen, C₁₋₆alkyl, -O-C₁₋₆alkyl, benzyl, phenyl and C₃₋₆cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents, and where said substituents are independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆alkyl and trifluoromethyl;

R¹² is selected from: hydrogen, C₁₋₆ alkyl, benzyl, phenyl and C₃₋₆cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents, and where said substituents are independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆alkyl, and trifluoromethyl;

R¹³ is selected from: hydrogen, C₁₋₆alkyl, -O-C₁₋₆alkyl, benzyl, phenyl and C₃₋₆cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents, and where said substituents are independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆alkyl and trifluoromethyl;

R¹⁴ is selected from: hydroxy, C₁₋₆ alkyl, -O-C₁₋₆alkyl, benzyl, phenyl, and C₃₋₆cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents, and where said substituents are independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆ alkyl and trifluoromethyl;

~~each-Z is independently selected from C and N; or N, where at most two of the Z are N;~~

R¹ is selected from:

- (a) hydrogen,
- (b) -C₁₋₆alkyl,
- (c) -C₀₋₆alkyl-O-C₁₋₆alkyl,
- (d) -C₀₋₆alkyl-S-C₁₋₆alkyl,
- (e) -(C₀₋₆alkyl)-(C₃₋₇cycloalkyl)-(C₀₋₆alkyl),
- (f) hydroxy,
- (g) heterocycle,
- (h) -CN,
- (i) -NR¹²R¹²,
- (j) -NR¹²COR¹³,
- (k) -NR¹²SO₂R¹⁴,
- (l) -COR¹¹,
- (m) -CONR¹²R¹², and
- (n) phenyl;

where said alkyl and cycloalkyl are unsubstituted or substituted with 1-7 substituents, and where said substituents are independently selected from: halo, hydroxy, -O-C₁₋₃alkyl, trifluoromethyl, C₁₋₃alkyl, -O-C₁₋₃alkyl, -COR¹¹, -SO₂R¹⁴, -NHCOCH₃, -NHSO₂CH₃, -heterocycle, =O, -CN, and where said phenyl and heterocycle are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -COR¹¹, C₁₋₃alkyl, C₁₋₃alkoxy and trifluoromethyl;

~~R² is selected from:~~

- ~~(a) —hydrogen,~~
- ~~(b) —C₁₋₃alkyl, optionally substituted with 1-3 fluoro,~~
- ~~(c) —O-C₁₋₃alkyl, optionally substituted with 1-3 fluoro,~~
- ~~(d) —hydroxy,~~
- ~~(e) —chloro,~~
- ~~(f) —fluoro,~~
- ~~(g) —bromo,~~
- ~~(h) —phenyl,~~
- ~~(i) —heterocycle, and~~
- ~~(j) —nothing or O (when the Z bonded to R² is N);~~

R³ is selected from:

- (a) hydrogen,
- (b) C₁₋₃alkyl, optionally substituted with 1-3 fluoro,
- (c) -O-C₁₋₃alkyl, optionally substituted with 1-3 fluoro,
- (d) hydroxy,
- (e) chloro,
- (f) fluoro,
- (g) bromo,
- (h) phenyl,
- (i) heterocycle, and
- (j) nothing or O (when the Z bonded to R³ is N);

~~R⁴ is selected from:~~

- ~~(a) —hydrogen,~~
- ~~(b) —C₁₋₃alkyl, optionally substituted with 1-3 fluoro,~~
- ~~(c) —O-C₁₋₃alkyl, optionally substituted with 1-3 fluoro,~~
- ~~(d) —hydroxy,~~
- ~~(e) —chloro,~~
- ~~(f) —fluoro,~~
- ~~(g) —bromo,~~
- ~~(h) —phenyl,~~
- ~~(i) —heterocycle, and~~

(j) ~~nothing or O (when the Z bonded to R⁴ is N);~~

R⁵ is selected from:

- (a) C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro and optionally substituted with hydroxyl,
- (b) -O-C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (c) -CO-C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (d) -S-C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (e) -pyridyl, which is unsubstituted or substituted with one or more substituents selected from: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹,
- (f) fluoro,
- (g) chloro,
- (h) bromo,
- (i) -C₄₋₆cycloalkyl,
- (j) -O-C₄₋₆cycloalkyl,
- (k) phenyl, which is unsubstituted or substituted with one or more substituents selected from: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹,
- (l) -O-phenyl, which is unsubstituted or substituted with one or more substituents selected from: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹,
- (m) -C₃₋₆cycloalkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (n) -O-C₃₋₆cycloalkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (o) -heterocycle,
- (p) -CN, and
- (q) -COR¹¹;

R⁶ is selected from:

- ~~— (a) — hydrogen,~~
- ~~— (b) — C₁₋₃alkyl, optionally substituted with 1-3 fluoro,~~
- ~~— (c) — O-C₁₋₃alkyl, optionally substituted with 1-3 fluoro,~~
- ~~— (d) — hydroxy,~~
- ~~— (e) — chloro,~~
- ~~— (f) — fluoro,~~
- ~~— (g) — bromo,~~
- ~~— (h) — phenyl,~~
- ~~— (g) — heterocycle, and~~
- ~~— (h) — nothing, when the Z bonded to R⁶ is N;~~

R⁷ is selected from:

- ~~(a) hydrogen,~~

- (b) ~~(C₀₋₆alkyl)-phenyl,~~
- (c) ~~(C₀₋₆alkyl)-heterocycle,~~
- (d) ~~(C₀₋₆alkyl)-C₃₋₇cycloalkyl,~~
- (e) ~~(C₀₋₆alkyl)-COR¹¹,~~
- (f) ~~(C₀₋₆alkyl)-(alkene)-COR¹¹,~~
- (g) ~~(C₀₋₆alkyl)-SO₃H,~~
- (h) ~~(C₀₋₆alkyl)-W-C₀₋₄alkyl,~~
- (i) ~~(C₀₋₆alkyl)-CONR¹²-phenyl,~~
- (j) ~~(C₀₋₆alkyl)-CONR²⁰-V-COR¹¹, and~~
- (k) ~~nothing, when X is O, S, or SO₂;~~

~~where W is selected from: a single bond, O, S, SO, SO₂, CO, CO₂, CONR¹² and NR¹², where V is selected from C₁₋₆alkyl or phenyl,~~

~~where R²⁰ is hydrogen, C₁₋₄alkyl or is joined via a 1-5 carbon tether to one of the carbons of V to form a ring, where the C₀₋₆alkyl is unsubstituted or substituted with 1-5 substituents,~~

~~where said substituents are independently selected from: halo, hydroxy, C₀₋₆alkyl, O-C₁₋₃alkyl, trifluoromethyl, and C₀₋₂alkyl-phenyl,~~

~~where the phenyl, heterocycle, cycloalkyl, and C₀₋₄alkyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from: halo, trifluoromethyl, hydroxy, C₁₋₃alkyl, O-C₁₋₃alkyl, C₀₋₃-COR¹¹, CN, NR¹²R¹², CONR¹²R¹², and C₀₋₃-heterocycle, or where the phenyl and heterocycle are fused to another heterocycle, which itself is unsubstituted or substituted with 1-2 substituents independently selected from hydroxy, halo, COR¹¹, and C₁₋₃alkyl,~~

~~and where alkene is unsubstituted or substituted with 1-3 substituents which are independently selected from: halo, trifluoromethyl, C₁₋₃alkyl, phenyl, and heterocycle;~~

R⁸ is selected from:

- (a) — hydrogen,
- (b) — nothing when X is either O, S, SO₂ or N or when a double bond joins the carbons to which R⁷ and R¹⁰ are attached,
- (c) — hydroxy,
- (d) — C₁₋₆alkyl,
- (e) — C₁₋₆alkyl hydroxy,

- (f) ~~O-C₁₋₃alkyl,~~
- (g) ~~COR¹¹,~~
- (h) ~~CONR¹²R¹², and~~
- (i) ~~CN;~~

~~or where R⁷ and R⁸ are be joined together to form a ring which is selected from:~~

- (a) 1H-indene,
- (b) 2,3-dihydro-1H-indene,
- (c) 2,3-dihydro-benzofuran,
- (d) 1,3-dihydro-isobenzofuran,
- (e) 2,3-dihydro-benzothiofuran,
- (f) 1,3-dihydro-isobenzothiofuran,
- (g) 6H-cyclopenta[d]isoxazol-3-ol
- (h) cyclopentane, and
- (i) cyclohexane,

where the ring formed is unsubstituted or substituted with 1-5 substituents independently selected from: halo, trifluoromethyl, hydroxy, C₁₋₃alkyl, -O-C₁₋₃alkyl, -C₀₋₃-COR¹¹, -CN, -NR¹²R¹², -CONR¹²R¹², and -C₀₋₃-heterocycle, and

~~or where R⁷ and R⁹ or R⁸ and R¹⁰ are joined together to form a ring which is phenyl or heterocycle, where said ring is unsubstituted or substituted with 1-7 substituents, where said substituents are independently selected from: halo, trifluoromethyl, hydroxy, C₁₋₃alkyl, O-C₁₋₃alkyl, COR¹¹, CN, NR¹²R¹², and CONR¹²R¹²;~~

R⁹ and R¹⁰ are independently selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) C₁₋₆alkyl,
- (d) C₁₋₆alkyl-COR¹¹,
- (e) C₁₋₆alkyl-hydroxy,
- (f) -O-C₁₋₃alkyl, and
- (g) =O, when R⁹ or R¹⁰ is connected to the ring via a double bond, and
- (h) halo;

~~R¹⁵ is hydrogen or C₁₋₆alkyl, which is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, CO₂H, CO₂C₁₋₆alkyl, and O-C₁₋₃alkyl;~~

~~R¹⁶ is selected from:~~

- ~~(a) — hydrogen,~~
- ~~(b) — C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 ———— substituents~~
~~where the substituents are selected from: fluoro, ———— C₁₋₃alkoxy, hydroxy, COR¹¹,~~
- ~~(c) — fluoro,~~
- ~~(d) — O-C₁₋₃alkyl, where alkyl is unsubstituted or substituted with 1-3 ———— fluoro, and~~
- ~~(e) — C₃₋₆cycloalkyl,~~
- ~~(f) — O-C₃₋₆cycloalkyl,~~
- ~~(g) — hydroxy,~~
- ~~(h) — COR¹¹,~~
- ~~(i) — OCOR¹³,~~

~~or R¹⁵ and R¹⁶ are joined together via a C₂₋₄alkyl or a
C₀₋₂alkyl-O-C₁₋₃alkyl chain to form a 5-7 membered ring;~~

~~R¹⁷ is selected from:~~

- ~~(a) — hydrogen,~~
- ~~(b) — C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 substituents, where said~~
~~substituents are selected from: fluoro, C₁₋₃alkoxy, hydroxy, —COR¹¹,~~
- ~~(c) — COR¹¹,~~
- ~~(d) — hydroxy, and~~
- ~~(e) — O-C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 substituents, where~~
~~said substituents are selected from: fluoro, C₁₋₃alkoxy, hydroxy, —COR¹¹,~~

~~or R¹⁶ and R¹⁷ are joined together by a C₁₋₄alkyl chain or a
C₀₋₃alkyl-O-C₀₋₃alkyl chain to form a 3-6 membered ring;~~

~~R¹⁸ is selected from:~~

- ~~(a) — hydrogen, and~~
- ~~(b) — C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,~~
- ~~(c) — fluoro,~~
- ~~(d) — O-C₃₋₆cycloalkyl, and~~
- ~~(e) — O-C₁₋₃alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,~~

~~or R¹⁶ and R¹⁸ are joined together by a C₂₋₃ alkyl chain to form a 5-6 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, COR¹¹, C₁₋₃ alkyl, and C₁₋₃ alkoxy;~~

~~or R¹⁶ and R¹⁸ are joined together by a C₁₋₂ alkyl-O-C₁₋₂ alkyl chain to form a 6-8 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, COR¹¹, C₁₋₃ alkyl, and C₁₋₃ alkoxy;~~

~~or R¹⁶ and R¹⁸ are joined together by a O-C₁₋₂ alkyl-O chain to form a 6-7 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, COR¹¹, C₁₋₃ alkyl, and C₁₋₃ alkoxy;~~

R¹⁹ is selected from:

- (a) — hydrogen;
- (b) — phenyl;
- (c) — C₁₋₆ alkyl which is substituted or unsubstituted with 1-6 of the — following substituents: COR¹¹, hydroxy, fluoro, chloro, O-C₁₋₃ alkyl;

~~or R² and R¹⁹ are joined together to form a heterocycle ring with a linker selected from:~~

- (a) — CH₂(CR²⁸R²⁸)₁₋₃;
- (b) — CH₂NR²⁹;
- (c) — NR²⁹CR²⁸R²⁸;
- (d) — CH₂O;
- (e) — CH₂SO₂;
- (f) — CH₂SO;
- (g) — CH₂S;
- (h) — CR²⁸R²⁸;

~~— where R²⁸ is selected from selected from:~~

- (a) — hydrogen;
- (b) — hydroxy;
- (c) — halo;
- (d) — C₁₋₃ alkyl, where the alkyl is unsubstituted or substituted with 1-6 substituents independently selected from: fluoro, and hydroxy;
- (e) — NR¹²R¹²;
- (f) — COR¹¹;
- (g) — CONR¹²R¹²;
- (h) — NR¹²COR¹³;
- (i) — OCONR¹²R¹²;

- (j) ~~NR¹²CONR¹²R¹²,~~
(k) ~~heterocycle,~~
(l) ~~CN,~~
(m) ~~NR¹²SO₂NR¹²R¹²,~~
(n) ~~NR¹²SO₂R¹⁴,~~
(o) ~~SO₂NR¹²R¹², and~~

~~(p) =O, where R²⁸ is connected to the ring via a double bond and the other R²⁸ at the same position is nothing, and~~

~~where R²⁹ is selected from: hydrogen, C₁₋₃alkyl, where the alkyl is unsubstituted or substituted with 1-6 substituents independently selected from: fluoro, hydroxy, COR¹³, SO₂R¹⁴, and SO₂NR¹²R¹²;~~

R²⁵ and R²⁶ are independently selected from:

- ~~(a) =O, where R²⁵ and/or R²⁶ is oxygen and is connected via a double bond,~~
~~(b) hydrogen,~~
~~(c) phenyl,~~
~~(d) C₁₋₆alkyl which is substituted or unsubstituted with 1-6 of the following substituents: COR¹¹, hydroxy, fluoro, chloro, O-C₁₋₃alkyl;~~

~~m is selected from 0, 1, or 2;~~

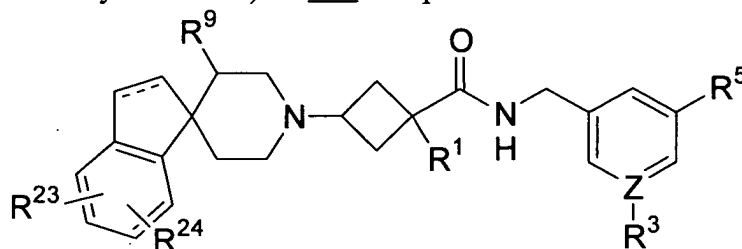
~~n is selected from 1 or 2;~~

~~the dashed line represents a single or a double bond;~~

~~and or a pharmaceutically acceptable salt or salts thereof and individual diastereomer diastereomers thereof.~~

Claims 2-5 (Canceled)

6. (Currently Amended) A The compound of Claim 1 of formula IId:



IId

wherein R^1 , R^3 , R^5 , R^9 , R^{23} , R^{24} , and Z are defined in Claim 1 and the dashed line represents a single or a double bond, and

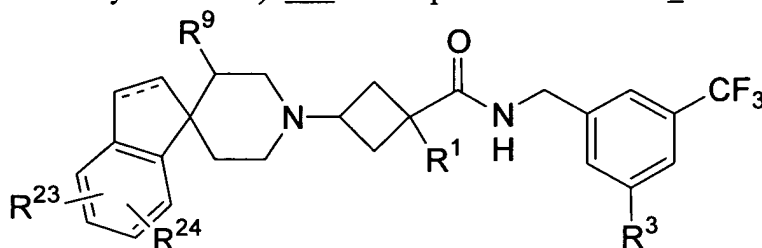
R^{23} and R^{24} are independently selected from:

- (a) hydrogen,
- (b) halo,
- (c) trifluoromethyl,
- (d) hydroxy,
- (e) C_{1-3} alkyl,
- (f) $-O-C_{1-3}$ alkyl,
- (g) $-C_{0-3}-CO_2H$,
- (h) $-C_{0-3}-CO_2C_{1-3}$ alkyl,
- (i) $-CN$, and
- (j) $-C_{0-3}$ -heterocycle,

and/or a pharmaceutically acceptable salts and salt or individual diastereomer diastereomers thereof.

Claim 7 (Canceled)

8. (Currently Amended) The A compound of Claim 1 of formula II f:



II f

wherein R^1 , R^3 , R^5 , R^9 , R^{23} , and R^{24} are defined in Claim 1,

and/or a pharmaceutically acceptable salts and salt or individual diastereomer diastereomers thereof.

9. (Currently amended) A The compound of Claim 8 wherein R^1 is selected from:

- hydrogen, phenyl, heterocycle, $-C_{1-6}$ alkyl, $-C_{0-6}$ alkyl- $O-C_{1-6}$ alkyl, and
- $-(C_{0-6}$ alkyl)-(C₃₋₇cycloalkyl)-(C₀₋₆alkyl),

where said alkyl, phenyl, heterocycle, and cycloalkyl are unsubstituted or substituted with 1-7 substituents, where said substituents are independently selected from:

- (a) halo,
- (b) hydroxy,

- (c) -O-C₁₋₃alkyl,
- (d) trifluoromethyl,
- (f) C₁₋₃alkyl,
- (g) -O-C₁₋₃alkyl,
- (h) -COR¹¹,
- (i) -CN,
- (j) -NR¹²R¹², and
- (k) -CONR¹²R¹².

10. (Currently amended) A The compound of Claim 9 wherein R¹ is selected from:

(1) -C₁₋₆alkyl, which is unsubstituted or substituted with 1-6 substituents where said substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl,
- (d) trifluoromethyl, and
- (e) -COR¹¹,

(2) -C₀₋₆alkyl-O-C₁₋₆alkyl-, which is unsubstituted or substituted with 1-6 substituents where said substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl, and
- (c) -COR¹¹,

(3) -(C₃₋₅cycloalkyl)-(C₀₋₆alkyl), which is unsubstituted or substituted with 1-7 substituents where said substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl,
- (d) trifluoromethyl, and
- (e) -COR¹¹, and

(4) phenyl or heterocycle which is unsubstituted or substituted with 1-3 substituents where said substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl,
- (d) trifluoromethyl, and
- (e) -COR¹¹.

11. (Currently amended) A The compound of Claim 10 wherein R¹ is selected from:

- (a) hydrogen,
- (b) C₁₋₆alkyl, which is unsubstituted or substituted with 1-6 substituents

independently selected from: fluoro and hydroxyl

- (c) phenyl, and
- (d) pyridyl.

12. (Currently amended) A The compound of Claim 6 wherein Z is C and R³ is selected from:

- (a) hydrogen
- (b) halo
- (c) hydroxy
- (d) C₁₋₃alkyl, where the alkyl is unsubstituted or substituted with 1-6 substituents

independently selected from: fluoro, and hydroxy,

- (e) -COR¹¹,
- (f) -CONR¹²R¹²,
- (g) -heterocycle,
- (h) -NR¹²-SO₂-NR¹²R¹²,
- (i) -NR¹²-SO₂-R¹⁴,
- (j) -SO₂-NR¹²R¹²,
- (k) -nitro, and
- (l) -NR¹²R¹².

13. (Currently Amended) A The compound of Claim 12 wherein Z is C, and R³ is selected from:

- (a) fluoro,
- (b) trifluoromethyl, and
- (c) hydrogen.

14. (Currently Amended) A The compound of Claim-~~8~~ 6 wherein R⁵ is selected from:

- (a) C₁₋₆alkyl substituted with 1-6 fluoro,
- (b) -O-C₁₋₆alkyl substituted with 1-6 fluoro,
- (c) chloro,
- (d) bromo, and
- (e) phenyl.

Claims 15-19 (Canceled)

20. (Original) A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

Claims 21 and 22 (canceled)

23. (Currently amended) A method for ~~treating, ameliorating, controlling or reducing the risk of~~ treating rheumatoid arthritis which comprises the administration to a patient of an effective amount of a the compound of Claim 1.

24 (New) The compound of Claim 1, which is selected from the following compounds, or a pharmaceutically acceptable salt or individual diastereomer thereof:

